Amendments to the Claims

Please amend the claims to read as follows:

1. (Currently Amended) A method of assessing relative susceptibility of a human to an undesirable bone density condition, the method comprising assessing occurrence in the human's genome of at least two disorder-associated polymorphisms (DAPs) including:

a DAP in a gene which encodes a protein that influences, by way of a transmembrane signaling pathway of a bone cell, expression of a component of bone matrix; and

a DAP in a gene which encodes a protein for which the level of expression of the protein is associated with bone resorption,

whereby occurrence of any of the ~~polymorphisms~~ DAPs is an indication that the human is more susceptible to an undesirable bone density condition than a human whose genome does not comprise the ~~polymorphism~~ DAP, and whereby occurrence of a plurality of the ~~polymorphisms~~ DAPs is an indication that the human is even more susceptible to an undesirable bone density condition than a human whose genome does not comprise the ~~polymorphisms~~ DAPs.

2-5. (Canceled)

6. (Previously Presented) The method of claim 1, wherein the bone cell is an osteoblast.

7. (Previously Presented) The method of claim 1, wherein the bone cell is an osteoclast.

8. (Currently Amended) The method of claim 1, wherein the genes are ~~selected from the group consisting of~~

i) ~~the gene which encodes parathyroid hormone (PtH);~~

~~ii) a gene which encodes a PtH receptor;~~

~~iii) the gene which encodes calcitonin;~~

~~iv) a gene which encodes a calcitonin receptor;~~

~~v)~~ a gene which encodes a vitamin D receptor; and

~~vi) the gene which encodes osteocalcin;~~

~~vii) the gene which encodes tumor necrosis factor alpha 1;~~

~~viii) a gene which encodes a tumor necrosis factor alpha 1 receptor;~~

~~ix) the gene which encodes the alpha 1 subunit of type 1 collagen;~~

~~x) a gene which encodes an estrogen receptor;~~

~~xi)~~ ii) the gene which encodes interleukin-6~~; and~~

~~xii) a gene which encodes an interleukin 6 receptor~~.

9. (Currently Amended) The method of claim 1, wherein the genes include a gene encoding one of a vitamin D receptor~~, transforming growth factor beta, an estrogen receptor,~~ and interleukin-6.

10. (Canceled)

11. (Withdrawn) The method of claim 57, wherein occurrence of the polymorphisms is assessed in at least four of the genes.

12. (Withdrawn) The method of claim 57, wherein occurrence of the polymorphisms is assessed in at least six of the genes.

13. (Canceled)

14. (Currently Amended) The method of claim 1, wherein occurrence of an individual disorder-associated polymorphism is assessed by

contacting a nucleic acid derived from the human's genome with a first oligonucleotide that anneals with higher stringency with the ~~disorder-associated polymorphism~~ DAP than with a corresponding ~~non-disorder-associated polymorphism~~ non-DAP and

assessing annealing of the first oligonucleotide and the nucleic acid,

whereby annealing of the first oligonucleotide and the nucleic acid is an indication that the human's genome comprises the~~-disorder-associated polymorphism~~ DAP.

15. (Original) The method of claim 14, wherein the first oligonucleotide is attached to a support.

16. (Original) The method of claim 15, wherein the support has a plurality of different first oligonucleotides attached thereto.

17. (Currently Amended) The method of claim 16, wherein the support has attached thereto at least two first oligonucleotides that anneal with higher stringency with the ~~disorder-associated polymorphisms~~ DAPs than with the corresponding ~~non-disorder-associated polymorphisms~~ non-DAPs.

18. (Currently Amended) The method of claim 16, wherein the support has attached thereto at least four first oligonucleotides that anneal with higher stringency with the ~~disorder-associated polymorphisms~~ DAPs than with the corresponding ~~non-disorder-associated polymorphisms~~ non-DAPs.

19. (Currently Amended) The method of claim 16, wherein the support has attached thereto at least six first oligonucleotides that anneal with higher stringency with the ~~disorder-associated polymorphisms~~ DAPs than with the corresponding ~~non-disorder-associated polymorphisms~~ non-DAPs.

20. (Original) The method of claim 14, wherein the first oligonucleotide is a molecular beacon oligonucleotide.

21. (Currently Amended) The method of claim 14, wherein occurrence of an individual ~~disorder-associated polymorphism~~ DAP is further assessed by

contacting the nucleic acid with a second oligonucleotide that anneals with higher stringency with a ~~non-disorder-associated polymorphism~~ non-DAP than with the corresponding ~~non-disorder-associated polymorphism~~ DAP and

assessing annealing of the second oligonucleotide and the nucleic acid,

whereby annealing of the second oligonucleotide and the nucleic acid is an indication that the human's genome does not comprise the ~~disorder-associated polymorphism~~ DAP.

22. (Original) The method of claim 21, wherein the second oligonucleotide is attached to a support.

23. (Original) The method of claim 22, wherein the first and second oligonucleotides are attached to the same support.

24. (Original) The method of claim 21, wherein the second oligonucleotide is a molecular beacon oligonucleotide.

25. (Original) The method of claim 24, wherein the first and second oligonucleotides are spectrally distinct molecular beacon oligonucleotides.

26. (Currently Amended) The method of claim 1, further comprising calculating a susceptibility score by summing, for each of the selected genes in which a ~~disorder-associated polymorphism~~ DAP occurs in the human's genome, the product of a constant and a correlation factor, wherein the correlation factor represents the fraction of humans heterozygous or homozygous for the ~~disorder-associated polymorphism~~ DAP who exhibit the corresponding disorder, whereby the susceptibility score represents the relative susceptibility of the human to an undesirable bone density condition.

27. (Original) The method of claim 26, wherein the same constant is used for each selected gene.

28-29. (Canceled)

30. (Currently Amended) The method of claim ~~57~~ 1, wherein at least one of the ~~polymorphisms~~ DAPs is a single nucleotide polymorphism (SNP).

31. (Original) The method of claim 30, wherein occurrence of a SNP is assessed by annealing a nucleic acid derived from the human's genome with a primer that is complementary to the region adjacent the SNP on its 3' side, extending the primer using a polymerase in order to add a nucleotide residue complementary to the SNP to the primer, and detecting the identity of the nucleotide residue complementary to the SNP.

32. (Original) The method of claim 31, wherein the nucleotide residue is a non-extendable residue.

33. (Currently Amended) The method of claim 30, wherein the SNP is selected from the group consisting of

a) ~~occurrence of a cytosine residue in the codon of the gene encoding transforming growth factor beta 1 protein corresponding to amino acid residue 10 of the protein, whereby the codon encodes proline;~~

~~b)~~ occurrence of a thymine residue 8 residues upstream of the normal start codon of the gene encoding vitamin D receptor, whereby the residue is part of an initiation codon and the gene encodes a variant vitamin D receptor comprising three additional amino acids at its amino terminus; and

~~c) occurrence of a nucleotide residue that is characteristic of apolipoprotein E polymorphic variant 4;~~

~~d) occurrence of a thymine residue in the gene encoding the alpha 1 subunit of type 1 collagen at a site at which a guanine residue normally occurs, whereby a recognition site for the transcription factor Sp1 is altered;~~

~~e)~~ b) occurrence of a cytosine residue at position -174 of the interleukin 6 gene promoter~~;~~

~~f) occurrence of guanine residue at the position at which a cytosine residue normally occurs in the codon corresponding to amino acid residue 986 of the calcium sensing receptor gene, whereby the codon encodes a serine residue;~~

~~g) occurrence of a thymine residue at the position corresponding to position +1417 of the cDNA encoding a PtH receptor;~~

~~h) occurrence of a thymine residue at the position at which a cytosine residue normally occurs in the codon corresponding to amino acid residue 447 of the calcitonin receptor gene, whereby the codon encodes a leucine residue;~~

~~i) occurrence of a thymine residue at position +1377 of the calcitonin receptor gene; and~~

~~j) occurrence of a cytosine residue where a guanine residue normally occurs at the first nucleotide position of intron 2 of the PtH gene~~.

34. (Withdrawn) The method of claim 1, wherein at least one of the polymorphisms is occurrence of a thymine-adenine repeat at position -1174 upstream of exon 1 of the estrogen receptor gene.

35. (Withdrawn) The method of claim 57, wherein at least one of the polymorphisms is occurrence of a tetranucleotide simple tandem repeat in intron 4 of the aromatase cytochrome P-450 gene.

36. (Withdrawn) The method of claim 57, wherein at least one of the polymorphisms is occurrence of a cytosine-adenine repeat at a position from 947 to 984 residues upstream of the transcription start site of the insulin growth factor 1 gene.

37-56. (Canceled)

57. (Withdrawn) The method of claim 1, comprising assessing occurrence in the human's genome of at least three disorder-associated polymorphisms in genes selected from the group consisting of:

a) genes which encode a protein component of bone matrix;

b) genes which encode an enzyme that catalyzes synthesis of an organic component of bone matrix;

c) genes which encode an enzyme that catalyzes deconstruction of an organic component of bone matrix;

d) genes which encode a protein that facilitates mineralization of bone matrix;

e) genes which encode a protein that facilitates de-mineralization of bone matrix;

f) genes which encode a protein that influences, by way of a transmembrane signaling pathway of a bone cell, expression of a protein selected from the group consisting of

i) a component of bone matrix;

ii) an enzyme that catalyzes synthesis of an organic component of bone matrix;

iii) an enzyme that catalyzes deconstruction of an organic component of bone matrix;

iv) a protein that facilitates mineralization of bone matrix; and

v) a protein that facilitates de-mineralization of bone matrix;

g) genes which encode a protein associated with vitamin D uptake or with vitamin D metabolism;

h) genes which encode a protein for which the level of expression of the protein is associated with bone erosion;

i) genes which encode a protein for which the level of expression of the protein is associated with bone resorption; and

j) genes which encode a protein for which the level of expression of the protein is associated with bone formation.

58. (Withdrawn) The method of claim 1, wherein the polymorphisms are selected from the group consisting of

a) occurrence of a thymine residue 8 residues upstream of the normal start codon of the gene encoding vitamin D receptor, whereby the residue is part of an initiation codon and the gene encodes a variant vitamin D receptor comprising three additional amino acids at its amino terminus;

b) occurrence of a thymine residue in the gene encoding the alpha 1 subunit of type 1 collagen at a site at which a guanine residue normally occurs, whereby a recognition site for the transcription factor Sp1 is altered;

c) occurrence of a cytosine residue at position -174 of the interleukin 6 gene promoter;

d) occurrence of guanine residue at the position at which a cytosine residue normally occurs in the codon corresponding to amino acid residue 986 of the calcium sensing receptor gene, whereby the codon encodes a serine residue;

e) occurrence of a thymine residue at the position corresponding to position +1417 of the cDNA encoding a PtH receptor;

f) occurrence of a thymine residue at the position at which a cytosine residue normally occurs in the codon corresponding to amino acid residue 447 of the calcitonin receptor gene, whereby the codon encodes a leucine residue;

g) occurrence of a thymine residue at position +1377 of the calcitonin receptor gene; and

h) occurrence of a cytosine residue where a guanine residue normally occurs at the first nucleotide position of intron 2 of the PtH gene.

59. (Previously Presented) The method of claim 1, wherein the gene which encodes a protein that influences, by way of a transmembrane signaling pathway of a bone cell, expression of a component of bone matrix is a gene which encodes a vitamin D receptor.

60. (Previously Presented) The method of claim 59, comprising detecting occurrence of a thymine residue 8 residues upstream of the normal start codon of the gene encoding the vitamin D receptor, whereby the residue is part of an initiation codon and the gene encodes a variant vitamin D receptor comprising three additional amino acids at its amino terminus.

61. (Previously Presented) The method of claim 1, wherein the gene which encodes a protein for which the level of expression of the protein is associated with bone resorption is the gene which encodes interleukin-6.

62. (Previously Presented) The method of claim 61, comprising detecting occurrence of a cytosine residue at position -174 of the interleukin 6 gene promoter.